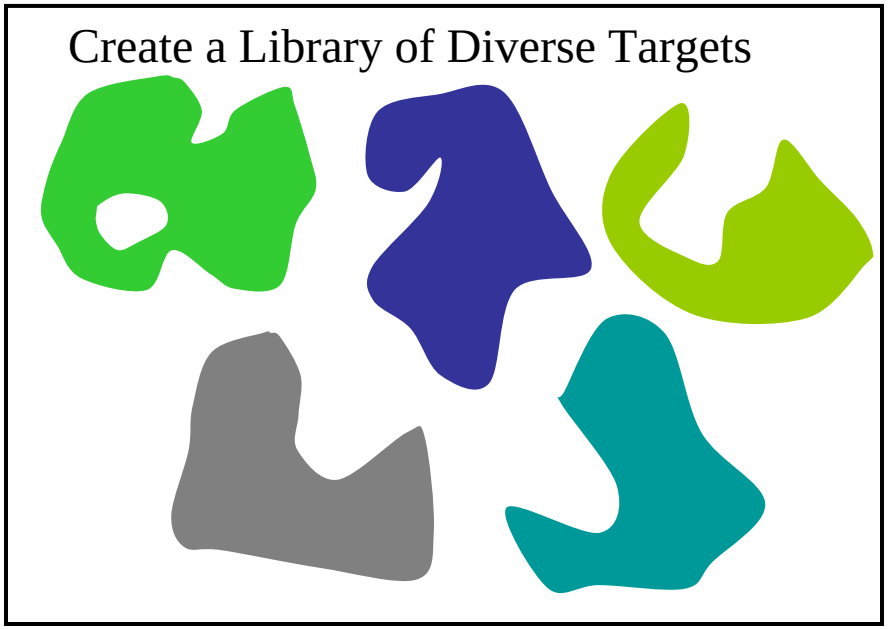
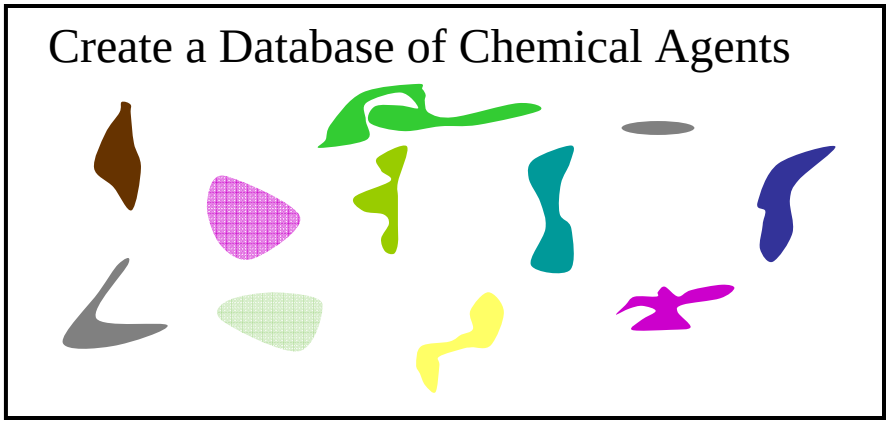
Virtual Screening for Chemical Toxicity: A Tool for Deriving Hypotheses and Determining Testing Priorities

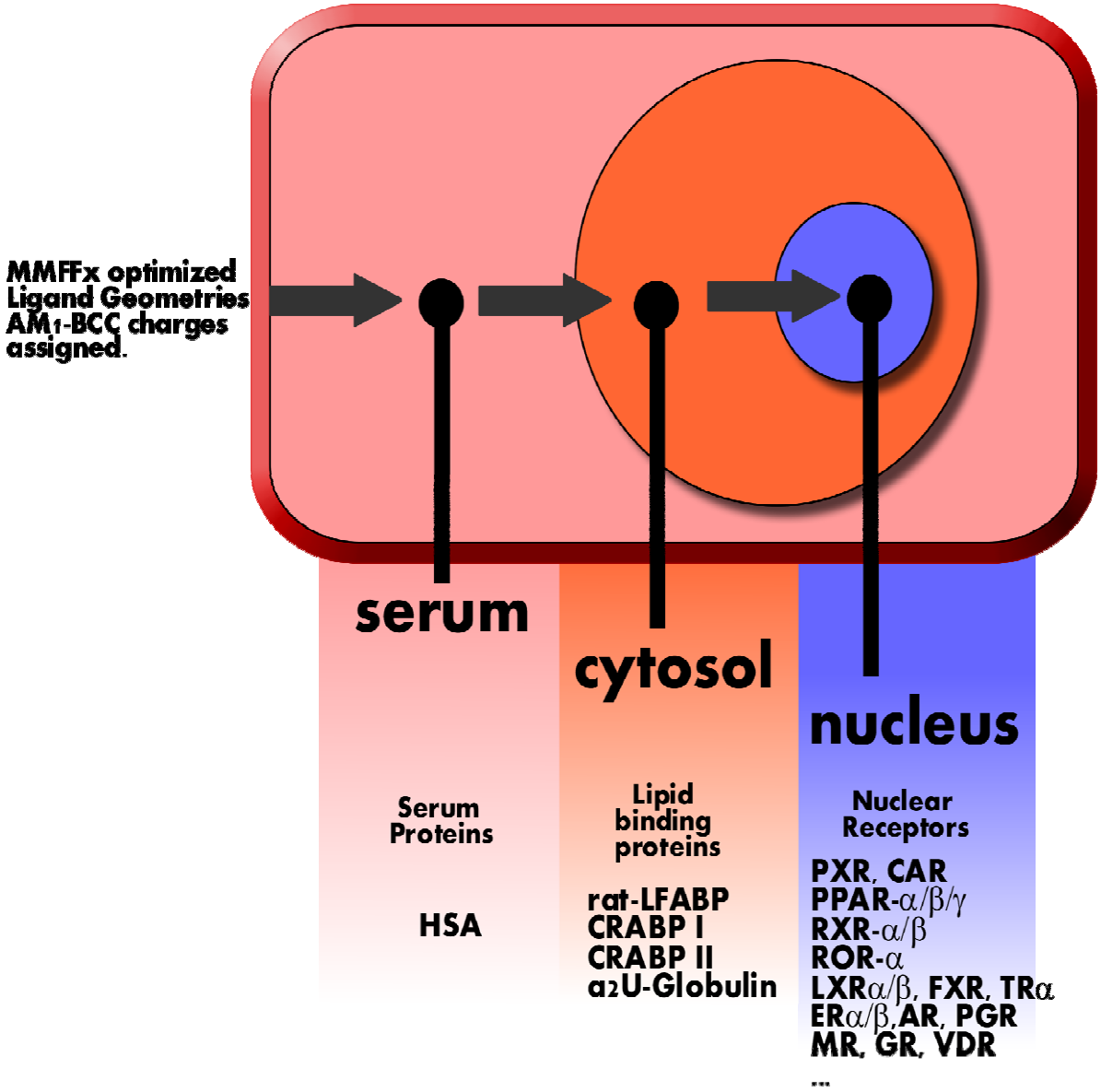
Virtual Screening Approach





- Can either:
  - *Screen a set of chemicals* over the entire target library
  - *Screen the database of chemicals* over a set of targets of interest (such as the hormone receptors)
- Assumes important targets are known – must be defined in the library
  - Library of binding site grids representing chemical/physical interactions
- Each chemical-target pair that has a docking score above a certain threshold will be *flagged* for experimental and/or computational testing
  - Will this method work for weak binders?

In Silico Structure-Based Chemical Prioritization Scheme



Virtual Toxicity Screening Tools

- The primary engine for the development of these tools is the pharmaceutical industry and the commercial need to develop new drugs.
- Important differences between these two applications
  - To become a drug lead a molecule must be strong actor while environmental agents are often weak actors.
  - It is a success to find a few agents - all or almost all of the active agents must be identified in a virtual Tox screen.
  - For toxicity screening false negatives are much more important than false positives. Many false positives can be tolerated as long as there are many true negatives.